Modern Concepts of Cardiovascular Disease

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Editor
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Associate Editor
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PROBLEMS IN THE EVALUATION OF PAIN IN THE CHEST*

Introduction

The cause of pain in the chest is easy to determine in patients who display typical clinical features. The discussion to follow will not deal with such instances, however, but only with atypical patterns that, although of frequent occurrence, may challenge the skill of the most astute diagnostician.

In the evaluation of atypical chest pain, adherence to certain concepts is of value. Among these are:

1. *Realization of the importance of a meticulous history.* Although knowledge of the location, radiation, intensity, quality and duration of the pain is of value, more significant is an understanding of the conditions which induce and relieve it.

2. *Laboratory findings should be discounted unless they integrate with the clinical picture.* The frequency of angina pectoris in patients with asymptomatic hiatal hernias represents a common example. This principle is especially important in relation to the electrocardiogram and will be discussed later.

3. *Study of a patient during a spontaneous attack of pain* will often provide an otherwise missing clue.

4. *Reproduction of the pain* is often the most valuable and sometimes the sole means of diagnosis.[1] In many instances, it is also an effective therapeutic procedure. When the patient realizes that the physician can induce and relieve the pain at will, he knows that his doctor understands his disorder. The confidence so engendered may be a cornerstone of successful therapy.

I. Problems in the Diagnosis of Angina Pectoris

1. *Angina without a clear history of relation to effort.* This is not unusual. Perhaps the most usual situation is that of a patient who takes little exercise, either because of a chosen sedentary life or because some coexisting disorder, such as emphysema or occlusive vascular disease of the legs, prevents sufficient exertion to induce anginal pain. Another reason is an inadequate history, failing to distinguish between the effects of effort after meals and the effect of meals alone. Some patients, believing their discomfort to be of digestive origin, will insist on the postprandial occurrence but, unless specifically questioned, will not state that this "indigestion" only occurs during exertion after meals, neither factor alone inducing it.

When a patient has attacks only at rest, an electrocardiogram recorded during the pain may be of crucial importance. A normal record so obtained does not exclude angina.

The recognition of angina occurring at rest is of especial importance because the impending infarction can be prevented in some instances by the vigorous use of coronary dilator drugs and of anticoagulants coupled with proper regulation of physical and emotional stress.

2. *Evaluation of the response to nitroglycerin.* The failure of this drug to produce immediate and complete relief of nonanginal pain, and its striking effect in the vast majority of anginal attacks, may be of great diagnostic import. However, one must guard against false negative responses due to inadequate dosage or deterioration of the drug, and against false positive results due to suggestion or to the *post hoc, ergo propter hoc* error in the mind of the patient. A statement that nitroglycerin does not relieve the pain can be made only when the dosage has been sufficient to produce undoubted pharmacological effects, *i.e.*, pounding headache or flushing of the face. Similarly, a positive statement that relief is obtained by the drug is only important when such relief is almost immediate (within one to five minutes), is complete, and is not duplicated by the sublingual administration of placebos, such as saccharin. In doubtful instances, the alterna-

* From the Department of Medicine, Medical College of Alabama, Birmingham, Alabama.

KANSAS CITY HEART ASS'N
406 W. 34th ST.
KANSAS CITY 11, MISSOURI

tive administration of these substances (recorded on a chart, giving the exact number of minutes elapsing between sublingual application and the cessation of pain) may be of great diagnostic significance.

3. *Value and limitation of special procedures in the diagnosis of angina pectoris.* The electrocardiogram, when properly used, is of definite value but its improper use is probably the most common cause of incorrect diagnosis.[2] This is not surprising when one considers the pressure under which physicians labor and realizes that it requires only a few minutes to record and misinterpret an electrocardiogram, as contrasted with the hours or days involved in a thorough clinical study.

Fixed changes in the electrocardiogram, even when marked, should be evaluated in relation to a possible history of trauma to the chest, with cardiac contusion or the innocent scar of healed pericarditis. Evanescent minor T-wave changes may be due to recent carbohydrate ingestion, with intracellular shift of potassium, or to emotional hyperventilation or release of epinephrine. Electrocardiographic changes after exercise must be interpreted with great caution. In our experience, postexertional depressions of the *S-T junction* of 1 mm., or even more, are not uncommon in healthy subjects, particularly in those who are unusually sedentary. In the absence of digitalis therapy, depression of *the entire S-T segment* of several millimeters following exercise nearly always indicates coronary disease. A sagging, down-sloping S-T segment, appearing after exercise and disappearing in a few minutes, is usually significant. In some patients, diagnostic electrocardiographic changes develop prior to pain during exercise, but the reverse appears to be more frequent. Since other disorders may occasionally cause pain during exertion (*vide infra*), the pain test is crucial only when it can be demonstrated that the amount of effort required to induce pain is consistently increased by nitroglycerin as compared to placebos.

The ballistocardiogram is apparently of value at present in the hands of a few experts with wide experience. After six years of study we are still unwilling to rely upon it in the diagnosis of angina, even as a test for the effect of smoking. There is much variability in different techniques and great uncertainty concerning normal limits and the effects of athletic training of a healthy subject in causing an "abnormal" record to become normal. We are optimistic about the long-

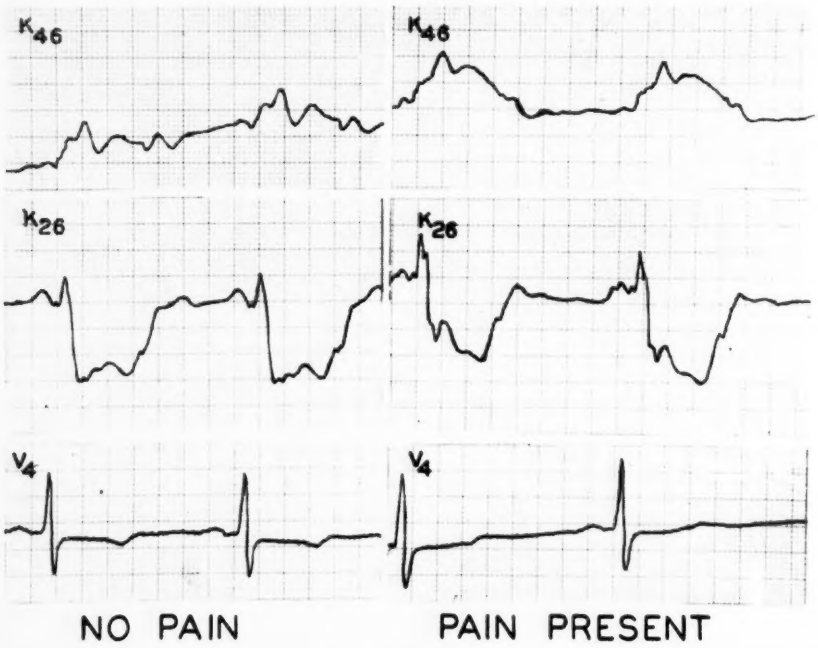

Figure 1. Camera speed 50 mm. per second. During the pain, the ECG from V_4 exhibited "improvement," *i.e.*, the T-wave inversion disappeared. The left parasternal trace (K_{26}) remained normal during ejection. The trace from the sixth interspace in the midclavicular line (K_{46}) was abnormal at rest, displaying predominant outward motion during ejection. When anginal pain was induced by pressure over the trigger area (see case report), this outward bulge became more pronounced. These observations, confirmed on several other occasions, seem to provide objective, as well as subjective, evidence for the concept of reflex coronary constriction as a precipitating cause of anginal attacks in this patient. It is deemed unlikely that this mechanism can cause angina unless there is organic disease with a limitation of the coronary reserve.

range value of the ballistocardiogram, but remain pessimistic about its present value in the diagnosis of angina pectoris.

The kinetocardiogram. There are some patients who, during anginal attacks, display temporary precordial bulges (Figure 1). These are apparently due to weakened contraction of ischemic muscle and correspond to the local ballooning, which may occur in experimental animals when a coronary artery is momentarily occluded. Occasionally, such bulges develop prior to the pain and without electrocardiographic changes.[3] However, this technique is at present of research value only. The uncertainties concerning methods and the limits of normal variation mentioned in relation to the ballistocardiogram are also applicable to the kinetocardiogram.

The diagnostic value of producing pain by exercise has been mentioned. Occasionally, vigorous exertion will fail to induce pain when a lesser effort undertaken under conditions of emotional stress, or after a large meal, or with ice cubes in the hands, or with a combination of these stimuli, will cause typical anginal distress. The especial significance of the demonstration of increased exercise tolerance after nitroglycerin has been mentioned above.

Since we believe that observation of the effect of nitroglycerin on the response to exercise is often of crucial diagnostic value, a few details of the procedure as we use it may be justified. The patient climbs up and down the usual two-step platform at a slow rate (6 round trips up and down, 24 steps per minute) for two minutes, having previously been instructed to cease the exercise should he develop even the slightest pain, ache, fullness, or discomfort of any type other than fatigue of the legs or dyspnea. A standard 12-lead electrocardiogram is taken before and immediately after the effort. If neither discomfort nor significant electrocardiographic changes develop, as explained above, more vigorous exercises are undertaken after a rest period of one or more hours between each test. Eventually, the patient, who has not had either pain or electrocardiographic changes with mild, moderate, or severe exercise, is pushed to maximal effort, *i.e.*, 12 round trips a minute for as many minutes as he can tolerate. If this effort does not induce pain or significant electrocardiographic changes, it is very unlikely that the coronary blood flow is impaired at the time of the test.*

Should a patient exhibit positive electrocardiographic changes (*i.e.*, depression of the entire S-T segment in one or more leads, or a well-marked sag of the segment) the test is considered positive, even though there is no pain. Should pain occur without impressive changes in the electrocardiogram, as is frequently the case, the same rate of exercise is repeated at intervals immediately after a sublingual placebo, such as saccharin, and immediately after a dose of nitroglycerin, which is sufficient to induce minor symptoms, such as pounding in the head or flushing. Each time the effort is continued until barely perceptible anginal discomfort appears. If it can be shown that the amount of exercise required to induce pain is consistently increased following nitroglycerin, the test is considered positive for inadequacy of the coronary circulation.

It should be emphasized that the hazard of this test is minimal, provided the following precautions are observed: 1) The patient stops the exercise as soon as he perceives the slightest discomfort (except dyspnea) in the chest, neck, arms, jaws or back. 2) If the effort induces frequent premature beats, or well-marked depression of the entire S-T segment, it is not repeated. 3) It is not increased in severity, but may be repeated if it causes sagging of the S-T segment. No attention is paid to depression of the S-T junction if such depression proceeds to an otherwise normal S-T and T. Utilizing these precautions, we have encountered no untoward results from more than a thousand exercise tests.†

4. *Exertional pain due to causes other than angina* is not uncommon. When such pain is aggravated by each breath, it is not of anginal origin. Some patients swallow air on walking and develop a feeling of tightness, which may be instantly relieved by belching. A few tense individuals hyperventilate during exertion and may develop a feeling of minimal constriction in the chest. The coexistence of paresthesia of the lips and extremities, frequent sighing and the reproducibility of the symptoms by voluntary hyperventilation, will serve as clues to this type of discomfort.

Patients with disorders that place a strain on the right ventricle may have a pain which is indistinguishable from angina, as regards location, quality, and relation to exercise.[4] The presence of mitral stenosis or extensive pulmonary disorders, the close association with dyspnea, the frequent presence of cyanosis plus clinical and other evidence of right ventricular hypertrophy, and the lack of a dramatic response to nitroglycerin, will usually identify this syndrome. It may actually represent "right ventricular angina,"[5] but, even so, the prognosis is less uncertain than in the usual type of angina and the treatment is aimed at the underlying disorder.

Pain arising in the skeletal tissues of the chest or arm may be related to effort,[6] although a pre-

* A normal response does not exclude atheroma, with a roughened coronary arterial wall which may lead to thrombosis and infarction in the near future. Only physiological impairment of the circulation can be detected by exercise tests, or any other procedure. There is no way of diagnosing roughening without narrowing, or even narrowing with complete compensation by collaterals.

† Since this paper was written, we have observed one fatality, occurring a few minutes after an exercise test.

cise history will often disclose that it is induced by a specific motion rather than by walking. In many instances, the pain comes with fatigue after an unusually tiring day, rather than during exertion. In rare cases, a pain in the left deltoid or pectoral region occurs during effort and can be shown to be due to the swing of the arm rather than the increased work of the heart. Similarly, certain patients with arthritis of the cervical or dorsal spine may have pain during walking which can be reproduced by specific motions. In all such instances, an erroneous diagnosis of angina may be made unless the history is obtained with unusual care and the skeletal tissues are thoroughly tested during the physical examination.

Finally, there are a few instances of skeletal pain which mimic angina almost completely. In such instances, the differentiation may be possible only by means of repeated observations of the effect of exercise, preceded alternatively by nitroglycerin and by placebos, or by the demonstration, after effort, of electrocardiographic changes which are so impressive as to be of undoubted significance.

5. *Reflex coronary constriction* probably never induces anginal pain in normal subjects. However, there is clinical and experimental evidence that such constriction may precipitate anginal attacks in patients who have both coronary disease and some other disorder in the same general area of the body. We have observed two patients with typical angina, whose pain and electrocardiographic changes could be produced by distending the coexistent hiatal hernia, as well as by exercise. The following case history illustrates how a coexisting skeletal disorder may act as such a trigger:

A 48-year-old diabetic woman had a striking family history of coronary heart disease. For four years, she had been subject to recurrent episodes of lancinating pain in the left pectoral region and dull substernal oppression, usually occurring together, although occasionally one would be present without the other. She was incapable of distinguishing between the pains as distinct entities, believing that they were related phenomena. The characteristic episodes consisted of a sharp pain in the fifth intercostal space, followed rapidly by the development of substernal pain radiating to the shoulders, arms, neck and jaws. This pain would come with effort and at rest, particularly if recumbent. She had initially been relieved by nitroglycerin, given sublingually, but for the past three months nitroglycerin had had little, if any, effect.

Physical examination showed moderate obesity, a large sustained apical impulse thought to be suggestive of a ventricular aneurysm, some tenderness of the second, third and fourth left costochondral joints, and pronounced tenderness of the fifth. There were no other relevant physical findings.

At rest, the electrocardiogram revealed QRS complexes within normal limits. The precordial T waves were inverted to V_4, diphasic in V_5 and very slightly upright in V_6. During pain, either spontaneous or induced by effort, the S-T segment would sag slightly and the T vector would rotate anteriorly, causing the previously inverted T in V_4 to become upright, with appropriate changes in other leads.

At rest, kinetocardiograms revealed a "bulge" pattern of ventricular aneurysm. Moderate pressure over the fifth costochondral joint repeatedly caused (1) severe local pain, (2) rapid development of substernal pain with radiation to the arms and jaws, (3) an increase in the aneurysmal bulge as recorded by the kinetocardiogram, and (4) the same electrocardiographic changes as those induced by effort. More severe local pain induced elsewhere, *i.e.*, compression of the thumbnail to the point of weeping, did *not* induce any chest pain or electrocardiographic changes. The electrocardiographic and kinetocardiographic changes are shown in Figure 1.

The most effective therapeutic measures proved to be those aimed primarily at the skeletal disorder, simultaneously treating the severe coronary disease with anticoagulants, low-fat diet, etc. Nitroglycerin, in doses of 1/25 gr., was effective in terminating the individual episodes.

The only reasonable conclusion that can be drawn from these observations is that the skeletal tissues were capable of initiating reflex coronary constriction and anginal attacks in a patient with advanced coronary disease. This concept fits well with the studies of Travell, *et al.*,[6] showing relief of the pain of myocardial ischemia by anesthetizing the chest wall.

6. *The frequent coexistence of skeletal and anginal pain* is one of the commonest causes of confusion. Aside from the referred pain of angina, with its characteristic response to effort and to nitroglycerin, pain in the chondrosternal or costochondral articulations, in the intercostal muscles, or in the arm, may be primary, *i.e.*, due to "rheumatism," or secondary, *i.e.*, due to changes in these tissues which are in some way induced by nerve impulses arising in the heart. Apparently such impulses may cause alterations in muscle tonus, as well as changes in blood flow and trophic alterations.

Whether primary or secondary, this pain clearly arises in the skeletal tissues and is not referred anginal pain. It is unaffected by walking with the hands in the pockets so the arms cannot swing. This pain is not relieved by nitroglycerin, but often is favorably affected by salicylates, warmth, local injections of procaine, and steroidal hormones. It is associated with local tenderness and with pain on local movement. It lasts for hours and, while usually mild, may be very severe. It is often a source of grave anxiety to the patient, who thinks it is "heart pain." Aside from the well-recognized frozen shoulder syndrome, this type of secondary skeletal pain is common in the pectoral and intercostal muscles, and especially frequent in the costochondral and chondrosternal junctions. Patients with early angina who have no evidence of a previous infarction may have this type of discomfort, which may mask the less annoying but more serious pain due to coronary disease. Any male beyond the age of 40, or any postmenopausal or diabetic female, complaining of such a "rheumatic" discomfort in the left pectoral region, shoulder or

arm, should be carefully studied with exercise tests before a diagnosis of primary skeletal pain is made.

II. Problems in the Diagnosis of Myocardial Infarction

Both because of space limitation, and because the diagnosis of infarction rests primarily on objective rather than subjective information, this topic will be considered very briefly.

Differentiation from pericarditis. In most instances of pericarditis, the fever precedes the pain, which is more aggravated by breathing than is the rule in patients with myocardial infarction. QRS changes are rare in patients with pericarditis, except when arteritis or collagen disease is the cause. The T-wave changes are similar in the two conditions, but are likely to be more widespread and somewhat less marked when pericarditis is responsible. It is probable, but unproved, that innocent pericardial scars, so common at autopsy (soldier's patches), are a frequent cause of focal minor electrocardiographic changes, often leading to an erroneous diagnosis of infarction. We have seen a number of patients who have had clinical evidence of pericarditis associated with localized changes in T waves. We suspect that this is the soldier's patch syndrome, but autopsy confirmation is lacking as the patients have remained in good health.

The differentiation between pulmonary embolism and myocardial infarction is usually not difficult because the former condition is often followed by infarction of the lung with pleural pain and hemoptysis. However, when the initial substernal pain of embolism, probably arising in the pulmonary artery or the right ventricle, is not followed by the typical manifestations of pulmonary infarction, and when the electrocardiogram is inconclusive, the differentiation may be impossible. Aside from embolism, other disorders, such as asthma, which produce an acute rise in pulmonary pressure and right ventricular strain, may induce pain and electrocardiographic changes which cannot readily be distinguished from those of infarction.

A dissecting aneurysm will usually be characterized by the progressive spread of pain, inequality of blood pressure and pulses, and other features. In most instances, the confusion with myocardial infarction arises during the initial hours. It persists chiefly in those patients in whom the pain does not spread, and where the involvement of the coronary ostia leads to electrocardiographic changes of ischemia or infarction.

Abdominal disorders, including pancreatitis, cholecystitis, and hiatal hernia, may mimic the pain of myocardial infarction. In most instances, serial daily electrocardiograms will resolve the initial uncertainty. A persistently normal sedimentation rate is strong evidence against infarction, but an elevated rate is of little specific value because most of the other conditions produce it also. The electrocardiogram, interpreted conservatively, without undue emphasis on minor T-wave changes, will be of diagnostic value in more than nine tenths of the instances of myocardial infarction. There is little parallelism, however, between the extent of the electrocardiographic change and the gravity of the clinical state, which is the proper guide to prognosis and therapy.

General Conclusions

In 90 to 95 per cent of patients with chest pain, a correct diagnosis can be made after careful study, often requiring several days. A correct decision as to whether or not coronary disease is the cause of the pain can probably be made in about 97 or 98 per cent. When one is certain that coronary disease is not causing the pain, an accurate diagnosis of the exact cause may be impossible in 10 to 15 per cent of patients, but this is rarely of much practical significance once coronary disease has been excluded. When there is doubt about a pain of prolonged nature and recent onset, the patient should be treated for myocardial infarction until the evidence clearly indicates that this condition is not present. In the person with recurrent pain of brief duration, and not of recent onset, the proper procedure is the opposite. In case of doubt, the patient should be reassured, but if there is any reasonable possibility of angina pectoris in the physician's mind, the instructions given the patient should be essentially the same as those for an individual with mild angina pectoris. In other words, such a person should live below the symptom threshold, but should be encouraged to exercise up to this threshold. Likewise, the standard instructions concerning emotional stress, weight reduction, and a low-fat diet, should be utilized. This can be done without psychic trauma by pointing out that the purpose of the instructions is to prevent future "heart trouble" rather than to treat disease already present.

The most important symptom in patients presenting cardiovascular problems is neither pain nor dyspnea, but fear. The physician's first consideration should be to avoid inducing it, and his second should be to do all he properly can to relieve it. The common and cardinal sins in treatment are the production by the physician of unnecessary anxiety and the institution of unwarranted restrictions. In most instances, these errors arise from a combination of a hastily-taken history and overemphasis of minor electrocardiographic changes. The time-consuming, thorough clinical study of the patient with pain

in the chest usually yields the doctor the satisfaction of certainty rather than guesswork, and *per se* constitutes the most valuable therapeutic measure for many patients.

T. J. REEVES, M.D.
Associate Professor of Medicine

T. R. HARRISON, M.D.
Professor of Medicine

Medical College of Alabama
Birmingham, Alabama

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